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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,989	12/14/2001	Peter David Davis	U 013589-7	1811

140 7590 03/26/2002

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EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
1642	7

DATE MAILED: 03/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/890,989	DAVIS, PETER DAVID	
<b>Examiner</b>	<b>Art Unit</b>		
Misook Yu	1642		

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 14 December 2001 and 12 February 2002.

2a)  This action is **FINAL**.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## **Disposition of Claims**

4)  Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1-20 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)  All b)  Some \* c)  None of:

1.  Certified copies of the priority documents have been received.
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)  The translation of the foreign language provisional application has been received.

15)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)  Notice of References Cited (PTO-892) 4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948) 5)  Notice of Informal Patent Application (PTO-152)  
3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6. 6)  Other: \_\_\_\_\_ .

## DETAILED ACTION

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 4-20 recite "vascular damaging agent" but it is not clear what the metes and bounds are for vascular damaging agent. ?

Claims 1-20 recite "inhibitor of the formation or action of nitric oxide" but it is not clear what the metes and bounds are for inhibitor of the formation or action of nitric oxide.

Claims 2 and 13 recite "amount sufficient to augment the effect of the vascular damaging agent", but it is not clear what the metes and bounds are for amount sufficient to augment the effect of the vascular damaging agent. *amounts*

Claim 11 provides for the use of a vascular damaging agent along with other active ingredients, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass.

A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. *cancelled*

Claim 11 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 12 provides for the use of inhibitor of formation or action of nitric oxide, but, since the claim does not set forth any steps involved in the method/process, it is unclear *cancelled*

what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 12 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). *Cancelled*

Claim 14 recites "substantially simultaneously but separately" but it is not clear what the metes and bounds are for "substantially simultaneously but separately". *Not addressed*

Claim 15 provides for the use of inhibitors of nitric oxide formation or action, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. *Cancelled*

Claim 15 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966)

Claim 4 recites the limitation "the nitric oxide synthase inhibitor". There is insufficient antecedent basis for this limitation in the claim. *fixed*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to *main fa*

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not describe as claimed "other than a cytokine releasing anticancer agent". The specification says that efficacy of vascular damaging agents could be improved by nitric oxide synthase inhibitor (page 2, third paragraph) and the examples of the vascular damaging agent are listed at page 3, the last paragraph. The specification does not describe "a vascular damaging agent other than a cytokine releasing anticancer agent".

**Priority**

This application repeats a substantial portion of foreign application GB9903404.3, filed 16 February, 1999, and adds additional disclosure (page 6, lines 6-18, and pages 7 and 8, Table 3 of the instant specification) not presented in the foreign application and the PCT and the GB documents do not describe the invention as claimed for the negative limitation "agent other than a cytokine releasing anticancer agent". The earlier documents do not reasonably convey an intention to claim everything except cytokine releasing anticancer agents. Therefore foreign priority is not granted to the contents of the instant specification at page 6, lines 6-18, and pages 7 and 8, Table 3. *Maintain*

**Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States. *Maintain*

Claims 1-5, 9-15, 16-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Tozer et al.

The claimed invention of the instant application is a composition comprising a vascular damaging agent (other than a cytokine releasing anticancer agent) and

inhibitors of the formation or action of nitric oxide (NO) for treatment of diseases involving active angiogenesis (claims 1-5 and 16-20); uses of the composition in the preparation of a medicament (claim 11, 12, 15); methods of treatment (claims 13 and 14) using the composition.

Tozer et al. (Cancer Res. April 1, 1999, 59, 1626-1634) teaches: 1) a composition (claims 1-10 and 16-20 of the instant application) comprising a vascular damaging agent other than a cytokine releasing anticancer agent together (CA-4-P) with a NO synthase inhibitor ( $N^w$ -nitro-L-arginine methyl ester) for treatment of diseases involving active angiogenesis; 2) uses of the composition in the preparation of a medicament (claim 11, 12, 15 of the); 3) methods of treatment (claims 13 and 14). See abstract and Fig. 6 of Tozer et al.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Narayanan et al and Stenger and WO-A-9509621 as applied to claim 1-5, 9-15, 16-20 above, and further in view of Tozer et al.

Stenger et al. (Eur. J. Pharmacol. 1995, 294, 703-12, see abstract only) teaches L-N6-1-iminoethyl-lysine. Narayanan et al teaches (J. Biol. Chem. 1995, 270, 11103-11, see abstract only) S-alkyl-L-thiocitrullines, and WO-A-9509621 teaches L-N-10, iminoethyl-ornithine. WO 95/09621, the document cited in the International Search Report (ISR) teaches a composition comprising NO synthase inhibitors, L-N6-1-iminoethyl-ornithine, in combination with a vascular damaging agent (cytokine-releasing anti-cancer agent) for the manufacture of a medicament for the treatment of cancer in a

mammal (page 3, third paragraph). Further, D2, D3, D4, D5, D6, D, D8 of ISR all disclose composition comprising a vascular damaging agent in combination with NO synthase, process of making and using the composition.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute one or more known NO synthase in conjunction with vascular damaging agent for treatment involving vascularization in the view of Tozer et al that administration of vascular damaging agent in presence of NO synthase inhibitor potentiated the effect of a vascular agent.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Misook Yu whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu

March 25, 2002

*Mary Mosher*  
MARY E. MOSHER  
PRIMARY EXAMINER  
GROUP 1800

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